In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application. This listing of claims is based on the claims pending as of the final Office Action mailed December 12, 2006:

1. (Currently Amended) A method for identifying ~~nucleic acid ligands~~ an aptamer that binds to a target molecule, wherein the ~~nucleic acid ligands~~ aptamer comprises a 2'-OMe modified nucleotide, comprising the following steps:

a) preparing a transcription reaction mixture comprising (i) a ~~mutated~~ modified RNA polymerase that is able to incorporate any one of a 2'-OMe modified nucleotide triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP, wherein said modified RNA polymerase comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), (iii) ~~wherein at least one NTP is a 2'-OMe NTP and at least one NTP is a~~ 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate a 2'-modified nucleotide triphosphate (2'-modified NTP) as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the NTP;

b) preparing a candidate mixture of single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the ~~mutated~~ modified RNA polymerase incorporates ~~at least one of~~ the ~~one or more~~ 2'-OMe modified NTPs into nucleic acid molecules of said candidate mixture;

c) contacting the candidate mixture with said target molecule;

d) partitioning the nucleic acids having an increased affinity to the target molecule relative to the candidate mixture from the remainder of the candidate mixture; and

e) amplifying the increased affinity nucleic acids, in vitro, to yield a ligand-enriched

mixture of nucleic acids, whereby ~~nucleic acid ligands of the target molecule~~ aptamers are identified.

2. - 4. (Cancelled)

5. (Currently Amended) The method of claim 1, wherein the ~~mutated~~ modified RNA polymerase is a ~~mutated~~ modified T7 RNA polymerase.

6. (Currently Amended) The method of claim 5, wherein the ~~mutated~~ modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

7. (Currently Amended) The method of claim 5, wherein the ~~mutated~~ modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

8. (Currently Amended) The method of claim 5, wherein the ~~mutated~~ modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

9. (Currently Amended) The method of claim 1, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

10. (Original) The method of claim 9, wherein the leader sequence comprises an all-purine leader sequence.

11. (Currently Amended) The method of claim 10, wherein the all-purine leader sequence has a length selected from the group consisting of ~~at least 6 nucleotides long;~~ at least 8 nucleotides

long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

12. (Currently Amended) The method of claim 1, wherein the transcription reaction mixture further comprises ~~manganese ions~~ inorganic pyrophosphatase.

13. (Currently Amended) The method of ~~claim 12~~ claim 1, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

14. (Currently Amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM, and the concentration of manganese ions is about 1.5 mM.

15. (Currently Amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM, and the concentration of manganese ions is about 2.0 mM.

16. (Currently Amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM, and the concentration of manganese ions is about 2.9 mM.

17. (Currently Amended) The method of claim 1, wherein the transcription reaction mixture further comprises a substituted ~~2'-OH~~ guanosine or ~~2'-OH~~ guanosine.

18. (Currently Amended) The method of claim 17, wherein the substituted ~~2'-OH~~ guanosine or guanosine is ~~2'-OH~~ GMP.

19. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises polyalkylene glycol.

20. (Previously Presented) The method of claim 19, wherein the polyalkylene glycol is

polyethylene glycol.

21. (Previously Presented) The method of claim 1 further comprising step

f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

22. - 76. (Cancelled)

77. (Currently Amended) The method of claim 1, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate ~~(ATP)~~, 2'-O-methyl cytidine triphosphate ~~(CTP) and~~, 2'-O-methyl uridine triphosphate ~~(UTP)~~ or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate ~~(GTP)~~ and 2'-OH guanosine triphosphate ~~(GTP)~~, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

78. (Currently Amended) The method of claim 1, wherein the ~~one or more oligonucleotide transcription templates are double stranded~~ transcription mixture further comprises spermidine, spermine or both spermidine and spermine.

79. (Currently Amended) The method of claim 6 or claim 7, wherein the transcription mixture further comprises ~~manganese ions~~ inorganic pyrophosphatase.

80. (Currently Amended) The method of claim ~~79~~ 130, wherein the transcription mixture further comprises ~~2'-OH~~ GMP.

81. (Previously Presented) The method of claim 80, wherein the oligonucleotide transcription template further comprises an all purine leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

82. (Currently Amended) The method of claim 81, wherein the all-purine leader sequence has a length selected from the group consisting of ~~at least 6 nucleotides long;~~ at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

83. (Currently Amended) The method of claim [[82]] 81, wherein the 2'-O-methyl modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate, and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

84. (Currently Amended) The method of claim 83, wherein the transcription mixture further comprises spermidine, spermine or both spermidine and spermine.

85. (Previously Presented) The method of claim 84, wherein the transcription mixture further comprises polyethylene glycol.

86. (Currently Amended) The method of claim 85, wherein the ~~one or more oligonucleotide transcription templates is double stranded~~ concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

87. (Previously Presented) The method of claim 86, further comprising step f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

88. (Currently Amended) The method of claim 8 or 101, wherein the transcription mixture further comprises ~~manganese ions~~ inorganic pyrophosphatase.

89. (Currently Amended) The method of claim [[88]] 131, wherein the transcription mixture further comprises ~~2'-OH~~ GMP.

90. (Previously Presented) The method of claim 89, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

91. (Currently Amended) The method of claim 90, wherein the all-purine leader sequence has a length selected from the group consisting of ~~at least 6 nucleotides long;~~ at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

92. (Currently Amended) The method of claim 91, wherein the 2'-O-methyl modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate, and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

93. (Currently Amended) The method of claim 92, wherein the transcription mixture further comprises spermidine, spermine or both spermidine and spermine.

94. (Previously Presented) The method of claim 93, wherein the transcription mixture further comprises polyethylene glycol.

95. (Currently Amended) The method of claim 94, wherein the ~~one or more oligonucleotide transcription templates is double stranded~~ concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

96. (Previously Presented) The method of claim 95, further comprising step f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

97. (Withdrawn) An aptamer composition comprising a sequence where substantially all adenosine nucleotides are 2′-O-methyl adenosine, substantially all cytidine nucleotides are 2′-O-methyl cytidine, substantially all guanosine nucleotides are 2′-O-methyl guanosine or deoxy guanosine, substantially all uridine nucleotides are 2′-O-methyl uridine, wherein less than about 10% of the guanosine nucleotides are 2'-OH guanosine.

98. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where at least 80% of all adenosine nucleotides are 2′-O-methyl adenosine, at least 80% of all cytidine nucleotides are 2′-O-methyl cytidine, at least 80% of all guanosine nucleotides are 2′-O-methyl guanosine, at least 80% of all uridine nucleotides are 2′-O-methyl uridine, and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.

99. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where at least 90% of all adenosine nucleotides are 2′-O-methyl adenosine, at least 90% of all cytidine nucleotides are 2′-O-methyl cytidine, at least 90% of all guanosine nucleotides are 2′-O-methyl guanosine, at least 90% of all uridine nucleotides are 2′-O-methyl uridine, and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.

100. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where 100% of all adenosine nucleotides are 2′-O-methyl adenosine. 100% of all cytidine nucleotides are 2′-O-methyl cytidine, 90% of all guanosine nucleotides are 2′-O-methyl guanosine, and 100% of all uridine nucleotides are 2′-O-methyl uridine and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.

101. (New) A method for identifying an aptamer that binds to a target molecule, wherein the aptamer comprises a 2'-OMe modified nucleotide, comprising the following steps:

a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that is able to incorporate any one of a 2'-OMe modified nucleotide

triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP, wherein said modified RNA polymerase comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, and (vi) one or more partially double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate a 2'-modified nucleotide triphosphate (2'-modified NTP) as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the NTP;

b) preparing a candidate mixture of single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the modified RNA polymerase incorporates the 2'-OMe modified NTPs into nucleic acid molecules of said candidate mixture;

c) contacting the candidate mixture with said target molecule;

d) partitioning the nucleic acids having an increased affinity to the target molecule relative to the candidate mixture from the remainder of the candidate mixture; and

e) amplifying the increased affinity nucleic acids, in vitro, to yield a ligand-enriched mixture of nucleic acids, whereby aptamers are identified.

102. (New) A method for transcribing an oligonucleotide, comprising the following steps:

a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that is able to incorporate any one of a 2'-OMe modified nucleotide triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP, wherein said modified RNA polymerase comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates , wherein the modified RNA polymerase

exhibits an increased ability to incorporate a 2'-modified nucleotide triphosphate (2'-modified NTP) as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the NTP; and

b) transcribing the one or more oligonucleotide transcription templates under conditions to generate a transcribed oligonucleotide, whereby the modified RNA polymerase incorporates the 2'-OMe NTPs into the transcribed oligonucleotide.

103. (New) The method of claim 102, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

104. (New) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

105. (New) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

106. (New) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

107. (New) The method of claim 102, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

108. (New) The method of claim 107, wherein the leader sequence is an all-purine leader sequence.

109. (New) The method of claim 108, wherein the all-purine leader sequence has a length selected from at least 8 nucleotides long, at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

110. (New) The method of claim 102, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

111. (New) The method of claim 110, wherein the substituted guanosine or guanosine is GMP.

112. (New) The method of claim 102, wherein the transcription reaction mixture further comprises a polyalkylene glycol.

113. (New) The method of claim 112, wherein the polyalkylene glycol is polyethylene glycol.

114. (New) The method of claim 102, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

115. (New) The method of claim 102, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

116. (New) The method of claim 102, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM, and the concentration of manganese ions is about 1.5 mM.

117. (New) The method of claim 102, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM, and the concentration of manganese ions is about 2.0 mM.

118. (New) The method of claim 102, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM, and the concentration of manganese ions is about 2.9 mM.

119. (New) The method of claim 102, wherein the one or more 2' modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-

methyl guanosine triphosphate and 2'OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

120. (New) The method of any one of claims 104, 105 or 106, wherein the transcription mixture further comprises inorganic pyrophosphatase.

121. (New) The method of claim 132, wherein the transcription mixture further comprises GMP.

122. (New) The method of claim 121, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

123. (New) The method of claim 122, wherein the leader sequence is an all-purine leader sequence.

124. (New) The method of claim 123, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

125. (New) The method of claim 123, wherein the 2'-O-methyl modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate, and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

126. (New) The method of claim 125, wherein the transcription mixture further comprises spermidine, spermine or both spermidine and spermine.

127. (New) The method of claim 126, wherein the transcription mixture further comprises

polyethylene glycol.

128. (New) The method of claim 127, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

129. (New) The method of claim 130, further comprising step f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

130. (New) The method of claim 79, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

131. (New) The method of claim 88, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

132. (New) The method of claim 120, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.